```
     FILE 'REGISTRY' ENTERED AT 00:23:29 ON 17 MAY 2004
L1             11 S 208989-61-1 OR 12083-48-6 OR 1277-47-0 OR 209471-71-6 OR 2094
L2             13 S L1 OR 116994-87-7 OR 88993-59-3

     FILE 'CAPLUS, WPIDS, MEDLINE, USPATFULL' ENTERED AT 00:26:20 ON 17 MAY
     2004

     FILE 'REGISTRY' ENTERED AT 00:26:30 ON 17 MAY 2004
                SET SMARTSELECT ON
L3           SEL L2 1- CHEM :      33 TERMS
                SET SMARTSELECT OFF

     FILE 'CAPLUS, WPIDS, MEDLINE, USPATFULL' ENTERED AT 00:26:32 ON 17 MAY
     2004
L4            991 S L3/BI
L5           1318 S L4 OR (VANADOC? OR CYCLOPENTADIENVANAD? OR CYCLOPENTADIENYLVA
L6             10 S L5 AND (ANGIOGEN? OR ANTIANGIOGEN? OR VASCULAR? OR ARTERY OR
L7              8 DUP REM L6 (2 DUPLICATES REMOVED)

=> d que
L1             11 SEA FILE=REGISTRY 208989-61-1 OR 12083-48-6 OR 1277-47-0 OR
                  209471-71-6 OR 209471-70-5 OR 209117-92-0 OR 208989-72-4 OR
                  208989-68-8 OR 208989-66-6 OR 208989-64-4 OR 208989-63-3
L2             13 SEA FILE=REGISTRY L1 OR 116994-87-7 OR 88993-59-3
L3                SEL  L2 1- CHEM :      33 TERMS
L4            991 SEA L3/BI
L5           1318 SEA L4 OR (VANADOC? OR CYCLOPENTADIENVANAD? OR CYCLOPENTADIENYL
                  VANAD? OR DICYCLOPENTADIENVANAD? OR DICYCLOPENTADIENYLVANAD?)
L6             10 SEA L5 AND (ANGIOGEN? OR ANTIANGIOGEN? OR VASCULAR? OR ARTERY
                  OR ARTERIES OR RETINA OR RETINAL OR HEMANGIOMA? OR ANGIOPLAST?
                  OR STENT OR ARTHROPATH? OR PROLIFERATIVE DISORDER? OR NEOVASCUL
                  AR? OR RETINOPATH? OR ATHERECTOM? OR DIABET?)
L7              8 DUP REM L6 (2 DUPLICATES REMOVED)
```

L7 ANSWER 1 OF 8 USPATFULL on STN
AN 2003:289328 USPATFULL
TI Indolizine compounds
IN Ono, Mitsunori, Lexington, MA, UNITED STATES
Przewloka, Teresa, Tewksbury, MA, UNITED STATES
James, David, Cambridge, MA, UNITED STATES
Chimmanamada, Dinesh, UNITED STATES
Lu, Rongzhen, UNITED STATES
Nagai, Masazumi, UNITED STATES
Koya, Keizo, Chestnut Hill, MA, UNITED STATES
Sun, Lijun, Harvard, MA, UNITED STATES
PI US 2003204090 A1 20031030
AI US 2003-388332 A1 20030313 (10)
RLI Continuation-in-part of Ser. No. US 2002-319401, filed on 12 Dec 2002, PENDING Continuation-in-part of Ser. No. US 2002-244088, filed on 13 Sep 2002, PENDING
PRAI US 2001-322020P 20010913 (60)
DT Utility
FS APPLICATION
LREP FISH & RICHARDSON PC, 225 FRANKLIN ST, BOSTON, MA, 02110
CLMN Number of Claims: 22
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2569
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention relates to compounds of Formula (I) ##STR1##

wherein Ring A, X, Y, Z, R.sub.1, R.sub.2 and R.sub.3 are defined herein. These compounds are useful for treating and preventing cancer, inflammatory disorders, autoimmune diseases and other conditions involving PDE4 or elevated levels of cytokines. This invention also relates to pharmaceutical compositions comprising at least one compound of Formula (I) and methods for treating and preventing cancer, inflammatory disorders, autoimmune diseases and other conditions involving PDE4 or elevated levels of cytokines.

SUMM . . . fever and myalgias due to infection. In addition, the compounds of the present invention are useful in the treatment of **diabetes** insipidus and central nervous system disorders, such as depression and multi-infarct dementia).

SUMM . . . tissues by the immune system may be permanent, as with destruction of insulin-producing cells of the pancreas in Type 1 **diabetes** mellitus. Specific autoimmune diseases that may be ameliorated using the compounds and methods of this invention include without limitation, autoimmune. . . disease, ulcerative colitis, primary biliary cirrhosis, and autoimmune hepatitis), autoimmune diseases of the endocrine glands (e.g., Type 1 or immune-mediated **diabetes** mellitus, Grave's disease. Hashimoto's thyroiditis, autoimmune oophoritis and orchitis, and autoimmune disease of the adrenal gland); and autoimmune diseases of. . .

SUMM . . . 5-ethynyluracil; abiraterone; aclarubicin; acylfulvene; adecypenol; adozelesin; aldesleukin; ALL-TK antagonists; altretamine; ambamustine; amidox; amifostine; aminolevulinic acid; amrubicin; amsacrine; anagrelide; anastrozole; andrographolide; **angiogenesis** inhibitors; antagonist D; antagonist G; antarelix; anti-dorsalizing morphogenetic protein-1; antiandrogen, prostatic carcinoma; antiestrogen; antineoplaston; antisense oligonucleotides; aphidicolin glycinate; apoptosis gene. . .

SUMM . . . D-24851 (Asta Medica), A-105972 (Abbott), Hemiasterlin, 3-BAABU (Cytoskeleton/Mt. Sinai School of Medicine, also known as MF-191), TMPN (Arizona State University), **Vanadocene** acetylacetonate, T-138026 (Tularik), Monsatrol, Inanocine (also known as NSC-698666), 3-IAABE (Cytoskeleton/Mt. Sinai School of Medicine), A-204197 (Abbott), T-607 (Tularik, also. . .

L7 ANSWER 2 OF 8 USPATFULL on STN
AN 2003:120830 USPATFULL
TI Gel-microemulsion formulations
IN Yiv, Seang, Woodbury, MN, UNITED STATES
Li, Mingshu, St. Paul, MN, UNITED STATES
D'Cruz, Osmond, Maplewood, MN, UNITED STATES
Uckun, Fatih M., White Bear Lake, MN, UNITED STATES
PI US 2003083314 A1 20030501
AI US 2001-957434 A1 20010919 (9)
RLI Continuation-in-part of Ser. No. WO 2000-US7419, filed on 19 Mar 2000, UNKNOWN
PRAI US 1999-125142P 19990319 (60)
DT Utility
FS APPLICATION
LREP MERCHANT & GOULD PC, P.O. BOX 2903, MINNEAPOLIS, MN, 55402-0903
CLMN Number of Claims: 73
ECL Exemplary Claim: 1
DRWN 6 Drawing Page(s)
LN.CNT 3045
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A pharmaceutical composition adapted for use as a spermicide, the composition comprising a gel-microemulsion comprising an oil-in-water microemulsion and a polymeric hydrogel. The gel-microemulsion can be used in a spermicidal method.

Also, a gel-microemulsion pharmaceutical composition adapted for use as a formulation base for additional therapeutic agents. Examples of additional agents include, anti-microbial agents and spermicidal agents. Such gel-microemulsions with additional therapeutic agents can be used in methods for appropriate therapeutic treatment.

Also, a gel-microemulsion pharmaceutical composition that is adapted for use as both a spermicide and formulation base for anti-microbial agents to provide a dual function contraceptive/anti-microbial formulation. Method of using such a composition as a dual function contraceptive/anti-microbial formulation are also included.
DETD [0041] **"Vanadocene"** is a metallocene including vanadium as the transition metal ion.
DETD . . . (IV) compounds disclosed therein. Examples of such vanadium (IV) compounds include organometallic cyclopentadienyl vanadium IV complexes. Preferred such compounds include: **vanadocene dichloride**, bis (methylcyclopentadienyl) vanadium dichloride, **vanadocene** dibromide, **vanadocene** diiodide, **vanadocene** diazide, **vanadocene** dicyanide, **vanadocene** dioxycyanate, **vanadocene** dithiocyanate, **vanadocene** diselenocyanate, **vanadocene** ditriflate, **vanadocene** monochloro oxycyanate, **vanadocene** monochloroacetonitrilo tetrachloro ferrate, **vanadocene** acetylacetonato monotriflate, **vanadocene** bipyridino ditriflate, **vanadocene** hexafluoro acetylacetonato monotriflate, **vanadocene** acetylhydroxamato monotriflate, and **vanadocene** N-phenyl benzohydroxamato monotriflate. Particularly preferred compounds include **vanadocene** diselenocyanate, and **vanadocene dichloride.**
DETD [0159] Some preferred vanadium (IV) catecholate complexes include "bent sandwich" **vanadocene** monocatecholate complexes having the following structure formula, or pharmaceutically acceptable salts thereof: ##STR19##
DETD [0162] Particularly preferred such compounds include **vanadocene** catecholate, **vanadocene** mono-tertbutyl catecholate, and **vanadocene** 1,3-diisopropyl catecholate.
DETD . . . for observation and analysis. Each of the three regions of vagina were examined for epithelial ulceration, edema, leukocyte

infiltration, and **vascular** congestion. The scores were assigned based on the scoring system of Eckstein et al., (Eckstein P, et al., J Reprod. . .

DETD . . . 2, range 0-3) [Table 14]. In contrast, all rabbits treated with 4% N-9 had epithelial ulceration, edema, leukocyte influx, and **vascular** congestion characteristic of inflammation (mean individual scores 1-3; total score 9, range 7 to 11) as quantitated by histological scoring. . . 3 .+-. 2*.dagger..dagger-dbl.

Lamina propria thickness	1 .+-. 1	2 .+-. 1
Leukocyte Infiltration	1 .+-. 1	3 .+-. 2
Vascular congestion	0	1 .+-. 1
Total score	2 .+-. 1.dagger.	9 .+-. 2

*Seven rabbits were administered intravaginally with 1 ml. . .

DETD . . . for observation and analysis. Each of the three regions of vagina were examined for epithelial ulceration, edema, leukocyte infiltration, and **vascular** congestion. The irritation scores were assigned based on the scoring system of Eckstein et al (J. Reprod. Fertil., 1969, 20:. . .

DETD . . . total score 5) [Table 22]. None of the six rabbits treated with GM-144 revealed epithelial ulceration, edema, leukocyte influx, and **vascular** congestion characteristic of inflammation as quantitated by histological scoring according to the method of Eckstein et al. (J. Reprod. Fertil.,. . . propria thickness 1 .+-. 1.sup.b,c 1 .+-. 1 1 .+-. 1

Leukocyte Infiltration	2 .+-. 1	2 .+-. 1	2 .+-. 1
Vascular congestion	2 .+-. 1	2 .+-. 1	2 .+-. 1
Total score	5 .+-. 1	5 .+-. 1	5 .+-. 1

.sup.aSix. . .

CLM What is claimed is:

30. The composition of claim 29, wherein the organometallic cyclopentadienyl vanadium IV complexes is selected from the following: **vanadocene dichloride**, bis(methylcyclopentadienyl)vanadium dichloride, **vanadocene** dibromide, **vanadocene** diiodide, **vanadocene** diazide, **vanadocene** dicyanide, **vanadocene** dioxycyanate, **vanadocene** dithiocyanate, **vanadocene** diselenocyanate, **vanadocene** ditriflate, **vanadocene** monochloro oxycyanate, **vanadocene** monochloroacetonitrilo tetrachloro ferrate, **vanadocene** acetylacetonato monotriflate, **vanadocene** bipyridino ditriflate, **vanadocene** hexafluoro acetylacetonato monotriflate, **vanadocene** acethydroxamato monotriflate, and **vanadocene** N-phenyl benzohydroxamato monotriflate.

L7 ANSWER 3 OF 8 USPATFULL on STN
AN 2003:92693 USPATFULL
TI Dendritic-antineoplastic drug delivery system
IN Malik, Navid, Killburn, UNITED KINGDOM
Duncan, Ruth, London, UNITED KINGDOM
Tomalia, Donald A., Midland, MI, UNITED STATES
Esfand, Roseita, Mt. Pleasant, MI, UNITED STATES
PI US 2003064050 A1 20030403
AI US 2001-16733 A1 20011029 (10)
RLI Continuation-in-part of Ser. No. US 2001-881126, filed on 14 Jun 2001, PENDING Division of Ser. No. US 1998-111232, filed on 7 Jul 1998, ABANDONED
PRAI US 1997-51800P 19970707 (60)
DT Utility
FS APPLICATION
LREP THE DOW CHEMICAL COMPANY, INTELLECTUAL PROPERTY SECTION, P. O. BOX 1967, MIDLAND, MI, 48641-1967
CLMN Number of Claims: 19

ECL Exemplary Claim: 1
DRWN 18 Drawing Page(s)
LN.CNT 1344
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Antineoplastic dendritic polymer conjugates which are useful drug delivery systems for carrying antineoplastic agents to malignant tumors are prepared by obtaining a dendritic polymer having functional groups which are accessible to an antineoplastic agent capable of interacting with the functional groups, and contacting the dendritic polymer with the antineoplastic agent. The preferred platin-based analogues of the antineoplastic agents conjugated to the dendritic polymer may be administered intravenously, orally, parentally, subcutaneously, intramuscularly, intraarterially or topically to an animal having a malignant tumor in an amount which is effective to inhibit growth of the malignant tumor. The antineoplastic dendritic polymer conjugates exhibit high drug efficiency, high drug carrying capacity, good water solubility, good stability on storage, reduced toxicity, and improved anti-tumor activity in vivo.

SUMM . . . to dendritic polymer conjugates which are useful drug delivery systems for carrying cisplatin, carboplatin, oxaliplatin, tetraplatin, platinum-DACH, ormaplatin, titanocene dichloride, **vanadocene dichloride**, niobocene dichloride, molybdenocene dichloride, rhenocene dichloride, diorganotin dihalides or other metallocene dihalides (hereinafter "antineoplastic dendritic polymer conjugates"); preferably cisplatin and. . .

DETD . . . and the tumor has a large incoming blood flow and it will not leak to the surrounding area as the **vascular** size leaving the tumor is more restricted and the dendrimer size too large for those vessels. Thus a high concentration. . .

DETD . . . before. Examples of such antineoplastic agents include, but are not limited to, cisplatin, carboplatin, oxaliplatin, tetraplatin, platinum-DACH, ormaplatin, titanocene dichloride, **vanadocene dichloride**, niobocene dichloride, molybdenocene dichloride, rhenocene dichloride, diorganotin dihalides or other metallocene dihalides. The preferred antineoplastic agent is a platinum containing. . .

CLM What is claimed is:

. . . polymer conjugate of claim 1, wherein the dendritic polymer is conjugated to cisplatin, carboplatin, oxaliplatin, tetraplatin, platinum-DACH, ormaplatin, titanocene dichloride, **vanadocene dichloride**, niobocene dichloride, molybdenocene dichloride, rhenocene dichloride, diorganotin dihalides or other metallocene dihalides as the antineoplastic agent.

L7 ANSWER 4 OF 8 USPATFULL on STN
AN 2003:291180 USPATFULL
TI Vanadium compounds as anti-proliferative agents
IN Uckun, Faith M, White Bear Lake, MN, United States
Navara, Christopher S, Plymouth, MN, United States
PA Parker Hughes Institute, Roseville, MN, United States (U.S. corporation)
PI US 6642221 B1 20031104
AI US 2000-713544 20001115 (9)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Pak, John
LREP Merchant & Gould P.C.
CLMN Number of Claims: 7
ECL Exemplary Claim: 1
DRWN 0 Drawing Figure(s); 0 Drawing Page(s)
LN.CNT 1000
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Vanadium compounds as anti-proliferative agents. These compounds act to disrupt mitotic and meiotic spindle formation and thus are useful to

prevent cell mitosis (proliferation) and meiosis.

SUMM . . . are underway to develop new anti-proliferative agents for use as therapies in the treatment of cancer, as well as non-cancer **proliferative disorders** such as epithelial hyperplasia, polycytemia, erythrocytemia, thrombocytemia, EBV transformed lymphoproliferative syndrome, dysplastic nevus syndrome, restenosis after **angioplasty** for coronary heart disease, mastocytosis, histiocytosis, psoriasis, polyps, and the like. One target for anti-proliferative agents is the mitotic pathway.. . .

SUMM **Vanadocene dichloride** (VDC) has been shown to arrest tumor cell growth (Kopf-Maier, et al, J. Cancer Res. Clin. Onccol., 106: 44-52. 1983),. . .

SUMM . . . administering to a subject a effective mitosis or meiosis disrupting amount of a vanadium compound, preferably a vanadium cyclopentadienyl compound (**vanadocene**), or an oxovanadium compound. Exemplary compounds useful in the method of the invention are described, for example, in published PCT. . .

SUMM . . . useful applications where disruption of meiosis or mitosis is advantageous, for example, the treatment and prevention of cancer and non-cancer **proliferative disorders** including those described above, as well as in any other applications where the inhibition of mitosis and/or meiosis in cells. . .

SUMM The present invention is drawn to the use of vanadium compounds, preferably vanadium cyclopentadienyl compounds (**vanadocenes**) and oxovanadium compounds, including, but not limited to those described in published PCT applications WO99/36063; WO 00/27389; and WO 00/35930. Vanadium compounds useful in the method invention include **vanadocene** compounds such as **vanadocene dichloride** (VDC), vandocene acetylacetonate (VDacac), and those vanadium compounds shown below. Specifically, the present invention relates to the finding that these. . . and meiosis. The anti-mitotic and anti-meiotic activity makes these compounds particularly attractive anti-proliferative agents, particularly for the treatment of non-cancer **proliferative disorders**.

SUMM **"Vanadocene"** is a compound having a central vanadium metal ion coordinated with at least two cyclopentadiene groups.

SUMM "Non-cancer **proliferative disorder**" includes such disorders as non-cancer **proliferative disorders** such as epithelial hyperplasia, polycytemia, erythrocytemia, thrombocytemia, EBV transformed lymphoproliferative syndrome, dysplastic nevus syndrome, restenosis after **angioplasty** for coronary heart disease, mastocytosis, histiocytosis, psoriasis, polyps, and the like.

SUMM

Group A: **Vanadocene** dihalides
VDC **Vanadocene dichloride** (Cp.sub.2VCl.sub.2)
VMDC Bis (methyl cyclopentadienyl) vanadium dichloride [(MeCp).sub.2VCl.sub.2)
VDB **Vanadocene** dibromide (Cp.sub.2VBr.sub.2)
VDI **Vanadocene** diiodide (Cp.sub.2VI.sub.2)
Group B: **Vanadocene** di-pseudohalides
VDA **Vanadocene** diazide [Cp.sub.2V(N.sub.3).sub.2]
VDCN **Vanadocene** dicyanide (Cp.sub.2V(CN).sub.2)
VDOCN **Vanadocene** dioxycyanate (Cp.sub.2V(OCN).sub.2)
VDSCN **Vanadocene** dithiocyanate (Cp.sub.2V(SCN).sub.2)
VDSeCN **Vanadocene** diselenocyanate (VCp.sub.2(SeCN).sub.2)
Group C: **Vanadocene** disubstituted derivatives
VDT **Vanadocene** ditriflate (Cp.sub.2V(O.sub.3SCF.sub.3).sub.2)
VDCO **Vanadocene** monochloro oxycyanate (Cp.sub.2V(OCN)(Cl))
VDFe **Vanadocene** monoacetonitrilo monochloro tetrachloro ferrate (Cp.sub.2VClNCCH.sub.3)FeCl.sub.4
Group D: Chelated **Vanadocene** Complexes
VDacac **Vanadocene** acetylacetonato monotriflate (Cp.sub.2V(CH.sub.3COCH.sub.2COCH.sub.3)(O.sub.3SCF.sub.3)

VDBPY **Vanadocene** bipyridino ditriflate
(CP.sub.2V(C.sub.10H.sub.8N.sub.2)(O.sub.3SCF.sub.3).sub.2)
VDHfacac **Vanadocene** hexafluoro acetylacetonato monotriflate
Cp.sub.2V(CF.sub.3COCH.sub.2COCF.sub.3)(O.sub.3SCF.sub.3))
VDH **Vanadocene** acethydroxamato monotriflate
(Cp.sub.2V(CH.sub.3CON(O)H)(O.sub.3SCF.sub.3)
VDPH **Vanadocene** N-phenyl benzohydroxamato monotriflate
(Cp.sub.2V(C.sub.6H.sub.5CON(O)C.sub.6H.sub.5)(O.sub.3SCF.sub.3)
Group E. Oxovanadium Compounds
[(VO(phen)] = (diaqua)(1,10-phenanthroline)oxovanadium (IV) sulfate;
[VO(phen).sub.2] = (aqua)bis(1,10-phenanthroline)oxovanadium (IV) sulfate;
[VO(Me.sub.2-phen)] = (diaqua)(4,7-dimethyl-1,10-phenanthroline)-
oxovanadium (IV) sulfate;
[VO(Me.sub.2-phen).sub.2] =. . .
DETD The mitotic spindles of vehicle-treated and **vanadocene**-treated BT-20 breast cancer cells was examined using confocal laser scanning microscopy. Vehicle-treated control cells showed mitotic spindles that were organized. . .
CLM What is claimed is:
7. A method for treating a non-cancer **proliferative disorder** in a subject, comprising administering to the subject an effective mitosis inhibiting amount of a vanadium compound of structure II:. . .

L7 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 1
AN 2001:275687 CAPLUS
DN 135:220738
TI X-ray structure, solution properties, and biological activity profile of **vanadocene**(IV) acetylacetonate complex, [VCp2(acac)](CF3SO3): a dual-function anti-cancer agent with anti-**angiogenic** and anti-mitotic properties
AU Ghosh, P.; Ghosh, S.; Navara, C.; Narla, R. K.; Benyumov, A.; Uckun, F. M.
CS Department of Chemistry, Parker Hughes Institute, Parker Hughes Cancer Center, St. Paul, MN, 55113, USA
SO Journal of Inorganic Biochemistry (2001), 84(3-4), 241-253
CODEN: JIBIDJ; ISSN: 0162-0134
PB Elsevier Science Inc.
DT Journal
LA English
AB The structure of [V(.eta.5-C5H5)2(CH3C(O)CHC(O)CH3)](O3SCF3) (1) (=[VCp2(acac)](O3SCF3)), a dual-function anti-cancer agent with anti-**angiogenic** and anti-mitotic properties, was detd. by single-crystal X-ray diffraction. The geometry is well described as a pseudo-tetrahedral like structure with the centroids of the cyclopentadienyl rings and the two oxygen atoms of the acetylacetonate ring in the ancillary positions of the central vanadium (IV) atom. The bisector of the V(acac) fragment deviates from the C2 axis of the ligand framework by only 4.degree., compared to a deviation of 7.degree. for the V(acac) fragment in the tetramethylethano-bridged **vanadocene** acetyl acetonate complex. Crystal data for 1: space group, P21/c; a=7.5544(9) A, b=14.936(2) A, c=16.193(2) A, .beta.=102.901(2).degree., V=1781.0(4) A3; Z=4; R=0.0506 for 2310 reflections with I>2.sigma.(I). This report also details the ESR, UV/Vis spectroscopy, electrochem. properties and the biol. activity profile of this potent anti-cancer agent.
TI X-ray structure, solution properties, and biological activity profile of **vanadocene**(IV) acetylacetonate complex, [VCp2(acac)](CF3SO3): a dual-function anti-cancer agent with anti-**angiogenic** and anti-mitotic properties
AB The structure of [V(.eta.5-C5H5)2(CH3C(O)CHC(O)CH3)](O3SCF3) (1) (=[VCp2(acac)](O3SCF3)), a dual-function anti-cancer agent with anti-**angiogenic** and anti-mitotic properties, was detd. by single-crystal X-ray diffraction. The geometry is well described as a pseudo-tetrahedral like structure with. . . of the ligand framework by

only 4.degree., compared to a deviation of 7.degree. for the V(acac) fragment in the tetramethylethano-bridged **vanadocene** acetyl acetonate complex. Crystal data for 1: space group, P21/c; a=7.5544(9) A, b=14.936(2) A, c=16.193(2) A, .beta.=102.901(2).degree., V=1781.0(4) A3; Z=4;. . .

ST antitumor **vanadocene** acetylacetonate complex crystal structure

IT Mitosis
(inhibitors; properties and biol. activity of antitumor **vanadocene**(IV) acetylacetonate complex)

IT **Angiogenesis** inhibitors
Antitumor agents
Crystal structure
Cyclic voltammetry
ESR (electron spin resonance)
Stability
UV and visible spectra
(properties and biol. activity of antitumor **vanadocene**(IV) acetylacetonate complex)

IT **208989-61-1**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(properties and biol. activity of antitumor **vanadocene**(IV) acetylacetonate complex)

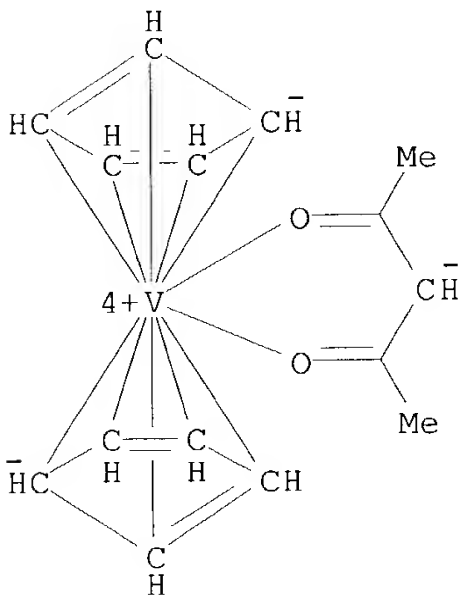
IT **208989-61-1**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(properties and biol. activity of antitumor **vanadocene**(IV) acetylacetonate complex)

RN 208989-61-1 CAPLUS

CN Vanadium(1+), bis(2,4-cyclopentadien-1-yl)(2,4-pentanedionato-.kappa.O,.kappa.O')-, salt with trifluoromethanesulfonic acid (1:1) (9CI) (CA INDEX NAME)

CM 1

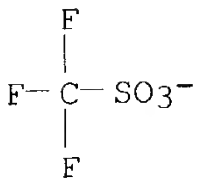
CRN 52895-18-8
CMF C15 H17 O2 V
CCI CCS



CM 2

CRN 37181-39-8

CMF C F3 O3 S



RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 2
AN 2001:39886 CAPLUS
DN 134:290506
TI Intravaginal Toxicity Studies of a Gel-Microemulsion Formulation of Spermicidal **Vanadocenes** in Rabbits
AU D'Cruz, Osmond J.; Uckun, Fatih M.
CS Department of Reproductive Biology, Parker Hughes Institute, St. Paul, MN, 55113, USA
SO Toxicology and Applied Pharmacology (2001), 170(2), 104-112
CODEN: TXAPA9; ISSN: 0041-008X
PB Academic Press
DT Journal
LA English
AB Bis-cyclopentadienyl complexes of vanadium(IV) or **vanadocenes** are rapid and potent inhibitors of human sperm motility with potential as a new class of contraceptive agents. We investigated the toxicity potential of intravaginally administered gel-microemulsion formulation of two representative **vanadocenes**, **vanadocene** acetylacetonato monotriflate (VDACAC) and **vanadocene** dithiocarbamate (VDDTC), in the rabbit model. New Zealand White rabbits in subgroups of three were exposed intravaginally to a gel-microemulsion with and without 0.1 or 0.25% VDACAC and VDDTC for 10 consecutive days. The doses of **vanadocenes** used were nearly 500- to 1250-fold and 2000- to 5000-fold higher than their resp. in vitro spermicidal EC50 values. Animals were euthanized on day 11 and vaginal tissues were evaluated for local toxicity by histopathol., cell proliferating activity by immunohistochem. detection of proliferating cell nuclear antigen (PCNA), and in situ apoptosis by the terminal deoxynucleotidyl transferase-mediated FITC-deoxyuridine triphosphate nick end-labeling (TUNEL) assay and confocal laser scanning microscopy (CLSM). Blood was analyzed for clin. chem. profiles. Vanadium content in selected organs and body fluids was detd. by at. absorption spectroscopy. None of the rabbits given 0.1% VDACAC and VDDTC intravaginally developed epithelial ulceration, edema, leukocyte influx, or **vascular** congestion characteristic of inflammation. Only minimal to moderate irritation was obsd. at 0.25% VDACAC and VDDTC. A significant decrease in epithelial and stromal PCNA expression was obsd. in the 0.25% dose group. However, TUNEL assay and CLSM revealed no staining in the vaginal epithelium and only minimal nonspecific staining in the stroma. Repetitive intravaginal application of 0.1 or 0.25% VDACAC and VDDTC had no adverse effects on clin. chem. profiles. Vanadium was not incorporated into rabbit tissues and body fluids at levels above 1 .mu.g/g. Thus, intravaginal administration of VDACAC and VDDTC at concns. nearly 500 and 2000 times higher than their resp. in vitro spermicidal EC50 values did not induce marked vaginal irritation, mucosal toxicity, or systemic absorption of vanadium in the rabbit model. The lack of significant mucosal or systemic toxicity of intravaginal **vanadocenes** obsd. may have particular clin. utility as a new class of contraceptive agents. (c) 2001 Academic Press.
TI Intravaginal Toxicity Studies of a Gel-Microemulsion Formulation of Spermicidal **Vanadocenes** in Rabbits

AB Bis-cyclopentadienyl complexes of vanadium(IV) or **vanadocenes** are rapid and potent inhibitors of human sperm motility with potential as a new class of contraceptive agents. We investigated the toxicity potential of intravaginally administered gel-microemulsion formulation of two representative **vanadocenes, vanadocene** acetylacetonato monotriflate (VDACAC) and **vanadocene** dithiocarbamate (VDDTC), in the rabbit model. New Zealand White rabbits in subgroups of three were exposed intravaginally to a gel-microemulsion with and without 0.1 or 0.25% VDACAC and VDDTC for 10 consecutive days. The doses of **vanadocenes** used were nearly 500- to 1250-fold and 2000- to 5000-fold higher than their resp. in vitro spermicidal EC50 values. Animals. . . at. absorption spectroscopy. None of the rabbits given 0.1% VDACAC and VDDTC intravaginally developed epithelial ulceration, edema, leukocyte influx, or **vascular** congestion characteristic of inflammation. Only minimal to moderate irritation was obsd. at 0.25% VDACAC and VDDTC. A significant decrease in. . . toxicity, or systemic absorption of vanadium in the rabbit model. The lack of significant mucosal or systemic toxicity of intravaginal **vanadocenes** obsd. may have particular clin. utility as a new class of contraceptive agents. (c) 2001 Academic Press.

ST spermicidal **vanadocene** intravaginal toxicity; vanadium complex spermicidal contraceptive toxicity

IT Vagina
(intravaginal toxicity studies of a gel-microemulsion formulation of spermicidal **vanadocenes** in rabbits)

IT Contraceptives
(spermicidal; intravaginal toxicity studies of a gel-microemulsion formulation of spermicidal **vanadocenes** in rabbits)

IT 7440-62-2D, Vanadium, bis-cyclopentadienyl complexes, biological studies **208989-61-1 209117-92-0**
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(intravaginal toxicity studies of a gel-microemulsion formulation of spermicidal **vanadocenes** in rabbits)

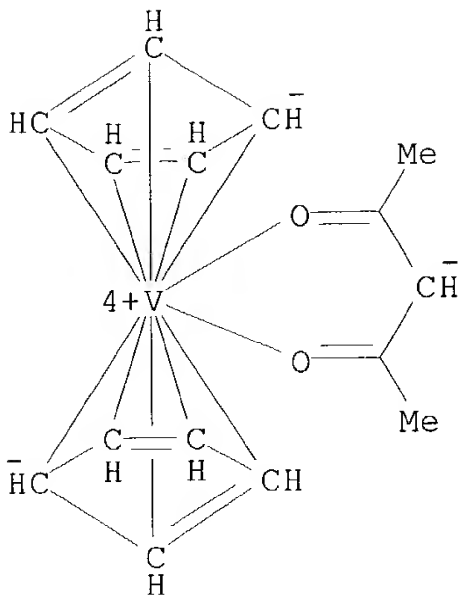
IT **208989-61-1 209117-92-0**
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(intravaginal toxicity studies of a gel-microemulsion formulation of spermicidal **vanadocenes** in rabbits)

RN 208989-61-1 CAPLUS

CN Vanadium(1+), bis(2,4-cyclopentadien-1-yl)(2,4-pentanedionato-.kappa.O,.kappa.O')-, salt with trifluoromethanesulfonic acid (1:1) (9CI) (CA INDEX NAME)

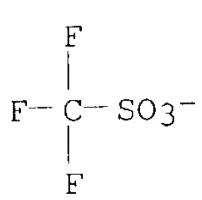
CM 1

CRN 52895-18-8
CMF C15 H17 O2 V
CCI CCS



CM 2

CRN 37181-39-8
CMF C F3 O3 S



RN 209117-92-0 CAPLUS
CN Vanadium(1+), bis(.eta.5-2,4-cyclopentadien-1-yl)(diethylcarbamodithioato-.kappa.S,.kappa.S')-, salt with trifluoromethanesulfonic acid (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 52676-10-5
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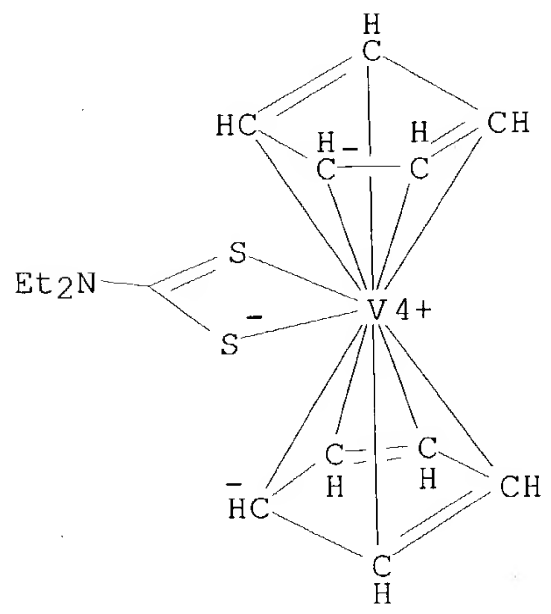
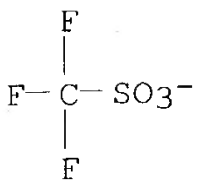
CCI CCS



CM 2

CRN 37181-39-8
CMF C F3 O3 S



RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 7 OF 8 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2000-672493 [65] WPIDS
DNC C2000-203619
TI Spermicidal composition comprises gel-microemulsion comprising oil-in-water microemulsion, polymeric hydrogel and optionally antimicrobial agent to provide dual contraceptive/antimicrobial function.
DC A96 B02 B03 B07
IN D'CRUZ, O; LI, M; UCKUN, F M; YIV, S
PA (PARK-N) PARKER HUGHES INST; (DCRU-I) D'CRUZ O; (LIMM-I) LI M; (UCKU-I) UCKUN F M; (YIVS-I) YIV S
CYC 93
PI WO 2000056366 A1 20000928 (200065)* EN 75
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000039038 A 20001009 (200103)
EP 1163009 A1 20011219 (200206) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
JP 2002540080 W 20021126 (200307) 104
US 2003083314 A1 20030501 (200331)
ADT WO 2000056366 A1 WO 2000-US7419 20000319; AU 2000039038 A AU 2000-39038 20000319; EP 1163009 A1 EP 2000-918179 20000319, WO 2000-US7419 20000319; JP 2002540080 W JP 2000-606270 20000319, WO 2000-US7419 20000319; US 2003083314 A1 Provisional US 1999-125142P 19990319, CIP of WO 2000-US7419 20000319, US 2001-957434 20010919
FDT AU 2000039038 A Based on WO 2000056366; EP 1163009 A1 Based on WO 2000056366; JP 2002540080 W Based on WO 2000056366
PRAI US 1999-125142P 19990319; US 2001-957434 20010919
AB WO 200056366 A UPAB: 20001214
NOVELTY - Pharmaceutical composition adapted for use as a spermicide comprises a gel-microemulsion comprising an oil-in-water microemulsion (I) and a polymeric hydrogel.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a pharmaceutical composition adapted for the topical delivery of a therapeutic agent comprising (a) a gel-microemulsion comprising (I) and a polymeric hydrogel and (b) a therapeutic agent, where the gel-microemulsion acts as a formulation base for the delivery of the therapeutic agent;

(2) delivering a therapeutically active agent to a subject comprising forming a pharmaceutical gel-microemulsion comprising (I), a polymeric hydrogel and the therapeutic agent, and administering the gel-microemulsion to the subject.

ACTIVITY - Spermicidal; antimicrobial.

USE - As gel-microemulsion formulation having spermicidal activity

and which can be used as vaginal contraceptive. The formulation may also act as a base for other therapeutic agents e.g. antimicrobial agents to give an antimicrobial formulation, spermicidal agents to enhance spermicidal effectiveness of the formulation, or to provide a dual function contraceptive/antimicrobial formulation for inhibiting transmission of sexually transmitted diseases e.g. AIDS, genital herpes, gonorrhea and chlamydia. The antimicrobial agents include antiviral, antibacterial and antifungal agents.

ADVANTAGE - Unlike commercially available detergent-type spermicides, the gel-microemulsion spermicide formulations are highly effective contraceptive agents with reduced levels of toxicity. Antimicrobial agents may be incorporated to prevent the transmission of diseases.

In an in vivo contraceptive activity test, none of the 16 rabbits administered a contraceptive formulation (GM-4) comprising (in wt.%): Captex 300 (lipid) (10.8), Cremophor El (surfactant) (7.6), Phospholipon 90G (phospholipid) (5.1), propylene glycol (humectant) (4.2), PEG-200 (humectant) (4.2), seaspan carrageenan (natural polymer) (0.9), viscarin carrageenan (natural polymer) (0.5), sodium benzoate (preservative) (0.2) and water (diluent) (66.5) intravaginally (using a 3 ml syringe) became pregnant after artificial insemination, compared to 15 out of 16 which became pregnant in a control group and delivered a total of 123 newborn rabbits. 5 out of 16 rabbits given Gynol II, a commercial contraceptive containing 2% nonoxynol-9 (N-9) became pregnant and delivered a total of 34 newborn rabbits. In addition, histological evaluation of 3 different regions of the vaginal tissue of 7 rabbits after daily intravaginal application of GM-4 for 10 consecutive days showed lack of significant vaginal irritation in all 7 rabbits examined. In contrast, all rabbits treated with 4% N-9 had epithelial ulceration, edema, leucocyte influx and **vascular** congestion characteristic of inflammation.

Dwg.0/5

AB . . .
in all 7 rabbits examined. In contrast, all rabbits treated with 4% N-9 had epithelial ulceration, edema, leucocyte influx and **vascular** congestion characteristic of inflammation.

Dwg.0/5

TECH. . .
group, preferably Br or Cl.

Preferred Vanadium(IV) Complex: The vanadium(IV) complex is an organometallic cyclopentadienyl vanadium(IV) complex or its salt, preferably **vanadocene dichloride**, bis(methylcyclopentadienyl) vanadium dichloride, **vanadocene** dibromide, **vanadocene** diiodide, **vanadocene** diazide, **vanadocene** dicyanide, **vanadocene** dioxycyanate, **vanadocene** dithiocyanate, **vanadocene** diselenocyanate, **vanadocene** ditriflate, **vanadocene** monochloro oxycyanate, **vanadocene** monochloroacetonitrilo tetrachloro ferrate, **vanadocene** acetylacetonato monotriflate, **vanadocene** bipyridino ditriflate, **vanadocene** hexafluoro acetylacetonato monotriflate, **vanadocene** bipyridino ditriflate, **vanadocene** hexafluoro acetylacetonato monotriflate, **vanadocene** acetylhydroxamato monotriflate or **vanadocene** N-phenyl benzohydroxamato monotriflate. The vanadium(IV) complex may also comprise an oxovanadium(IV) complex which preferably includes at least one bidentate ligand. . .

L7 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1975:544782 CAPLUS
DN 83:144782
TI Autoradiographic localization of organically bound iodine in the tunic of **vascular** stolon of Perophora orientalis, a compound ascidian
AU Fukumoto, Makoto
CS Dep. Gen. Educ., Nagoya City Univ., Nagoya, Japan
SO Kiyo - Nagoya-shiritsu Daigaku Kyoyobu, Shizen Kagaku-hen (1974), 20, 1-6
CODEN: NSKKAB; ISSN: 0465-7772

DT Journal
LA English
AB Fine filaments were obsd. in the tunic matrix which were aggregated in some places and dispersed in others. A relatively high concn. of Ag grains was obsd. over the regions where the fine filaments were aggregated. This suggested that the fine filaments in the tunic were responsible for binding I. A relatively high concn. of grains was also obsd. around the **vanadocyte** in the tunic. Thiourea, a potent goitrogen, eliminated grains almost completely from every component of the **vascular** stolon.
TI Autoradiographic localization of organically bound iodine in the tunic of **vascular** stolon of Perophora orientalis, a compound ascidian
AB . . . filaments in the tunic were responsible for binding I. A relatively high concn. of grains was also obsd. around the **vanadocyte** in the tunic. Thiourea, a potent goitrogen, eliminated grains almost completely from every component of the **vascular** stolon.